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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,720	07/20/2006	Claude V. Maina	NEB-238-PUS	4742

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,720	MAINA ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Preliminary Amendment filed July 20, 2006.

Claims 1-30 are pending in the instant application.

Claims 1-30 are subject to restriction as detailed below:

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 4 and 10, drawn to a method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the hsiRNA mixture, wherein the mutant RNase III is E38A, classifiable in class 435, subclass 6, for example.

II. Claim 4, drawn to a method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the hsiRNA mixture, wherein the mutant RNase III is E38T, classifiable in class 435, subclass 6, for example.

III. Claim 4, drawn to a method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the hsiRNA mixture, wherein the mutant RNase III is E38W, classifiable in class 435, subclass 6, for example.

IV. Claims 4 and 10, drawn to a method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a

mutant RNase III to produce the hsiRNA mixture, wherein the mutant RNase III is E65A, classifiable in class 435, subclass 6, for example.

V. Claim 13, drawn to a method of down-regulating gene expression of a target gene comprising preparing a heterogenous siRNA mixture containing dsRNA fragments from a preparation of large dsRNA by means of a mutant RNase III, causing dsRNA fragments from the siRNA mixture to degrade mRNA; and down-regulating gene expression of the target gene, wherein the mutant RNase III is E38A, classifiable in class 435, subclass 325, for example.

VI. Claim 13, drawn to a method of down-regulating gene expression of a target gene comprising preparing a heterogenous siRNA mixture containing dsRNA fragments from a preparation of large dsRNA by means of a mutant RNase III, causing dsRNA fragments from the siRNA mixture to degrade mRNA; and down-regulating gene expression of the target gene, wherein the mutant RNase III is E65A, classifiable in class 435, subclass 325, for example.

VII. Claim 28, drawn to a hsiRNA mixture, the mixture being capable of down regulating targeted gene expression in a cell, classifiable in class 536, subclass 24.5, for example. **If this Group is elected, a further restriction is required as detailed below.**

VIII. Claims 29 and 30, drawn to a composition comprising an RNase III having one or more mutations, wherein the one mutation is located at a position

corresponding to E38 in *E. Coli* RNase III in which the glutamic acid (E) has been mutated to an alanine (A), classifiable in class 536, subclass 23.1, for example.

Claims 1-3, 5-9, and 11 links the inventions of Groups I-IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 1-3, 5-9, and 11. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 12 and 14-27 links the inventions of Groups V and VI. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 12 and 14-27. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any

such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other, because of the following reasons:

Group VII is related to Groups V and VI as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the hsiRNA mixture capable of down regulating targeted gene expression in a cell of Group VII can be used in materially different process such as a hybridization probe in a method of identifying gene expression *in situ*, which is a materially different process than the methods of down-regulating gene expression of a target gene comprising preparing a heterogenous siRNA mixture containing dsRNA fragments from a preparation of large dsRNA by means of a mutant RNase III, causing dsRNA fragments from the siRNA mixture to degrade mRNA; and down-regulating gene expression of the target gene of Groups V and VI. Because these inventions are independent or distinct for the reasons

given above and there would be a serious burden on the Examiner if restriction were not required because the inventions require a different field of search (see MPEP 808.02), restriction for examination purposes as indicated is proper.

Groups I-IV are drawn to methods of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the hsiRNA mixture and are considered to be distinct from the methods of down-regulating gene expression of a target gene comprising preparing a heterogenous siRNA mixture containing dsRNA fragments from a preparation of large dsRNA by means of a mutant RNase III, causing dsRNA fragments from the siRNA mixture to degrade mRNA; and down-regulating gene expression of the target gene of Groups V and VI. The inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the methods of Groups I-IV are distinct from the methods of Groups V and VI since the methods of Groups I-IV recites distinct method steps and distinct objectives, apart from the method steps and objectives recited in Groups V and VI. Furthermore, Groups I-IV are distinct from Groups V and VI since the invention of Groups I-IV do not overlap in scope with that of Groups V and VI since each Group set recites materially distinct methods which differ in criteria for success. Because these Group sets utilize unique and different method steps, the inventions are also therefore not obvious variants, and have a materially different design. Furthermore, because

these Group sets utilize unique and different method steps, the prior art applicable to one Group set would not likely be applicable to another Group set and the inventions in each Group set are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph. Accordingly, restriction between these Groups is considered proper.

Group VII is drawn to a hsiRNA mixture, the mixture being capable of down regulating targeted gene expression in a cell and is considered to be distinct from the composition comprising an RNase III having one or more mutations, wherein the one mutation is located at a position corresponding to E38 in *E. Coli* RNase III in which the glutamic acid (E) has been mutated to an alanine (A) of Group VIII. The inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the hsiRNA mixture capable of down regulating targeted gene expression in a cell of Group VII is distinct from the composition comprising an RNase III having one or more mutations, wherein the one mutation is located at a position corresponding to E38 in *E. Coli* RNase III in which the glutamic acid (E) has been mutated to an alanine (A) of Group VIII for the following reasons: the inventions as claimed have a materially different design and mode of operation, function, and effect. For example, the hsiRNA mixture of Group VII comprises dsRNA fragments, while the composition comprising an RNase III having one or more mutations of Group VIII comprises enzymes, for example. Also, the hsiRNA

mixture of Group VII functions in a mode of down-regulating gene expression, while the composition comprising an RNase III having one or more mutations of Group VIII functions in a mode of cleaving dsRNA fragments to form hsiRNA mixtures. Because these Groups have different modes of operation and different effects, the inventions are therefore not obvious variants. Since it is a burden to search and examine these multiple inventions in a single application, due to the fact that the searches are divergent and non-coextensive, restriction is proper therefore. Furthermore, restriction for examination purposes as indicated is proper because the prior art applicable to one invention would not likely be applicable to the other invention.

Each of Groups I-IV is considered to be distinct, each from the other. The inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, although the methods recited in Groups I-IV are each methods of preparing a hsiRNA mixture, they are considered to be mutually exclusive from each other since each method uses a different and distinct RNase III mutant. For example, a search of the method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the hsiRNA mixture, wherein the mutant RNase III is E38A of Group I would likely not reveal art against a search of the method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the

hsiRNA mixture, wherein the mutant RNase III is E38T of Group II. Similarly, a search of the method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the hsiRNA mixture, wherein the mutant RNase III is E38W of Group III would likely not reveal art against a search of the method of preparing an hsiRNA mixture, comprising reacting a preparation of dsRNA with an effective amount of a mutant RNase III to produce the hsiRNA mixture, wherein the mutant RNase III is E65A of Group IV. Furthermore, the inventions of Groups I-IV II are considered to be mutually exclusive, each from the other since each Group is not disclosed as requiring any of the other respective Groups. Because these groups utilize unique structures, namely distinct RNase III mutations, the inventions are also therefore not obvious variants, and have a materially different design. Since it is a burden to search and examine these multiple inventions in a single application due to the fact that the searches are divergent and non-coextensive, restriction is proper therefore.

If Group VII is elected, claim 28 is subject to an additional restriction since it is not considered to be a proper genus/Markush. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580

F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claim 28 specifically claims a hsiRNA mixture, the mixture being capable of down regulating targeted gene expression in a cell, wherein the targeted gene is selected from a dozen or so target genes. Although the hsiRNA mixtures are capable of down regulating targeted gene expression, the instant hsiRNA mixtures are considered to be unrelated, since each hsiRNA mixture claimed targets a different and specific target gene, of a different and specific category, each gene having a different and specific GenBank Accession No. and different coordinate (As per Applicant's Table 1 in the instant specification at page 47). As such the Markush/genus of hsiRNA mixtures capable of down regulating targeted gene expression in claim 28 is not considered to constitute a proper genus, and is therefore subject to restriction. Furthermore, a search of more than one (1) of the hsiRNA mixtures capable of down regulating targeted gene expression claimed in claim 28 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed target genes. In view of the foregoing, one (1) target gene is considered to be a reasonable number for examination. Accordingly, if Applicants elect

Group VII, Applicants are required to elect **one (1)** target gene from claim 28. Note that this is not a species election but a restriction of distinct and independent inventions: unique and structurally distinct target nucleotide sequence genes.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper. Also, because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the Examiner if restriction were not required because the inventions require a different field of search (see MPEP 808.02), restriction for examination purposes as indicated is proper.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be

treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent

issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Terra Cotta Gibbs/
February 29, 2008

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/586,720	MAINA ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	